

1 What is Claimed is:

2 1. A chicken II GnRH analog, having the sequence p-Glu-His-Trp-Ser-His-Xaa-  
3 Trp-Tyr-Pro-Xaa<sup>2</sup>, capable of binding to tumor cell GnRH receptors and active in the presence of  
4 a post-proline peptidase or an endopeptidase, said analog comprising a D-amino acid substitution  
5 at position 6 and an ethylamide or aza-Gly-amide substitution at position 10.  
6

7 2. The chicken II GnRH analog of claim 1 wherein the chicken II GnRH analog is further defined  
8 as:

9 D-Arg(6)-chicken II GnRH-ethylamide; or

10 D-Arg(6)-chicken II GnRH-aza-Gly(10)-amide.  
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12 3. The chicken II GnRH analog of claim 1 wherein the post-proline peptidase is chorionic  
13 peptidase-1.  
14

15 4. The chicken II GnRH analog of claim 2 wherein the chicken II GnRH analog is further defined  
16 as D-Arg(6)-chicken II GnRH-aza-Gly(10)-amide having a sequence as defined in SEQ ID NO: 2  
17 (p-Glu-His-Trp-Ser-His-D-Arg-Trp-Tyr-Pro-aza-Gly-NH<sub>2</sub>).  
18

19 5. The chicken II GnRH analog of claim 1 wherein the chicken II GnRH analog is further defined  
20 as an aza-Gly(10)-amide Chicken II GnRH analog.  
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22 6. The chicken II GnRH analog of claim 1 wherein the chicken II GnRH analog is further defined

1 as comprising a D-Arg, a D-Leu, D-tBu-serine, or a D-Trp substitution at position 6 and an aza-  
2 Gly amide or an ethylamide at position 10.

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4 7. A pharmaceutical preparation comprising a compound according to claim 4, in admixture with  
5 a pharmaceutically acceptable carrier, diluent or excipient.

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7 8. A purified polypeptide, the amino acid sequence of which comprises SEQ ID NO: 2.

8 9. An antibody that binds specifically to the Chicken II GnRH polypeptide of SEQ ID NO: 6 or SEQ  
9 ID NO: 6 with at least one conservative amino acid substitution.

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11 10. The antibody of Claim 9 wherein said antibody is used in regulating cell proliferation.

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13 11. The antibody of Claim 9 wherein said antibody is used in the treatment of tumors.

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15 12. A method of determining whether a biological sample contains a chicken II GnRH polypeptide,  
16 comprising contacting the sample with the antibody of Claim 9 and determining whether the  
17 antibody specifically binds to the sample, said binding being an indication that the sample contains a  
18 chicken II GnRH polypeptide (SEQ ID NO: 6).

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20 13. An antibody that binds specifically to the receptor for the Chicken II GnRH polypeptide of SEQ  
21 ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution.

22  
23 14. The antibody of Claim 13 wherein said antibody is used in regulating cell proliferation.

24  
25 15. The antibody of Claim 13 wherein said antibody is used in the treatment of tumors.

26  
27 16. A method of determining whether a biological sample contains receptors for Chicken II GnRH

(SEQ ID NO: 6) comprising contacting the sample with the antibody of Claim 13 whether the antibody specifically binds to the sample, said binding being an indication that the sample contains receptors for Chicken II GnRH polypeptide (SEQ ID NO: 6).

17. A method of determining whether a biological sample contains the mRNA or DNA, or the respective complements thereof, that codes for Chicken II GnRH polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of subjecting said sample to in situ localization or any binding or hybridization procedure to determine whether said sample contains said mRNA or DNA.

18. The method of Claim 17 further comprising the step of monitoring cell function.

19. The method of Claim 17 further comprising the step of monitoring tumor growth.

20. A method of determining whether a biological sample contains the mRNA or DNA, or the respective complements thereof, that codes for the receptor to the Chicken II GnRH polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of subjecting said sample to in situ localization any binding or hybridization procedure to determine whether said sample contains said mRNA or DNA.

21. The method of Claim 20 further comprising the step of monitoring cell function.

22. The method of Claim 20 further comprising the step of monitoring tumor growth.

23. A method of regulating translation of mRNA with the sequence of SEQ ID NO:8 or a degenerate variant of SEQ ID NO:8 comprising the steps of:

providing a single stranded oligonucleotide at least 10 nucleotides in length, the oligonucleotide being complementary to a portion of SEQ ID NO:8 or a degenerate variant of SEQ

1 ID NO:8;

2 providing a cell comprising mRNA with the sequence of SEQ ID NO: 8 or a degenerate  
3 variant of SEQ ID NO: 8; and

4 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates translation  
5 of said mRNA in the cell.

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7 24. A method of regulating transcription of the sequence of SEQ ID NO: 1 or a degenerate variant of  
8 SEQ ID NO: 1 comprising the steps of:

9 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
10 oligonucleotide being complementary to a portion of SEQ ID NO: 1 or a degenerate variant of SEQ  
11 ID NO: 1;

12 providing a cell comprising a DNA with the sequence of SEQ ID NO: 1 or a degenerate  
13 variant of SEQ ID NO: 1; and

14 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates  
15 transcription of said DNA in the cell.

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17 25. A method of regulating translation of mRNA with the complement to the sequence of SEQ ID  
18 NO: 8 or a degenerate variant of SEQ ID NO: 8 comprising the steps of:

19 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
20 oligonucleotide having a portion of the sequence of SEQ ID NO: 8 or a degenerate variant of SEQ ID  
21 NO: 8 ;

22 providing a cell comprising mRNA with the complement to the sequence of SEQ ID NO: 8  
23 or a degenerate variant of SEQ ID NO: 8; and

24 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates translation  
25 of said mRNA in the cell.

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27 26. A method of regulating transcription of the complement to the sequence of SEQ ID NO: 1 or a  
28 degenerate variant of SEQ ID NO: 1 comprising the steps of:

29 providing a single stranded oligonucleotide at least 10 nucleotides in length, the

1 oligonucleotide having a portion of the sequence of SEQ ID NO: 1 or a degenerate variant of SEQ ID  
2 NO: 1;

3 providing a cell comprising a DNA with the complement to the sequence of SEQ ID NO: 1 or  
4 a degenerate variant of SEQ ID NO: 1; and

5 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates  
6 transcription of said DNA in the cell.

7 27. A method of regulating translation of mRNA with the sequence of SEQ ID NO: 8, the  
8 complement thereof, or a degenerate variant of SEQ ID NO: 8 or its complement comprising the  
9 steps of:

10 providing a polypeptide having the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
11 one conservative amino acid substitution;

12 providing a cell comprising mRNA with the sequence of SEQ ID NO: 8, the complement  
13 thereof, or a degenerate variant of SEQ ID NO: 8 or its complement; and

14 introducing the polypeptide into the cell, wherein the polypeptide regulates translation of said  
15 mRNA in the cell.

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17 28. A method of regulating transcription of the sequence of SEQ ID NO: 1, the complement  
18 thereof, or the degenerate variant of SEQ ID NO: 1 or its complement, comprising the steps of:

19 providing a polypeptide having the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
20 one conservative amino acid substitution;

21 providing a cell comprising a DNA with the sequence of SEQ ID NO: 1, the complement  
22 thereof, or the degenerate variant of SEQ ID NO: 1 or its complement; and

23 introducing the polypeptide into the cell, wherein the polypeptide regulates transcription of  
24 said DNA in the cell.

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26 29. A method of regulating the translation of mRNA for the receptor of the polypeptide with the  
27 sequence of SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative  
28 amino acid substitution or the DNA complement thereof comprising the steps of:

29 providing a single stranded oligonucleotide at least 10 nucleotides in length, the

oligonucleotide being complementary to a portion of SEQ ID NO: 1 or a degenerate variant of SEQ ID NO: 1;

providing a cell comprising mRNA for the receptor of the polypeptide with the sequence of SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative amino acid substitution or the DNA complement thereof; and

introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates the translation of said mRNA in the cell.

30. A method of regulating transcription of the DNA for the receptor of the polypeptide of SEQ ID NO: 6, the complement thereof, SEQ ID NO: 6 with at least one conservative amino acid substitution or its complement, comprising the steps of:

providing a single stranded oligonucleotide at least 10 nucleotides in length, the oligonucleotide having a portion of the sequence of SEQ ID NO: 1 or a degenerate variant of SEQ ID NO: 1;

providing a cell comprising DNA for the receptor of the polypeptide with the sequence of SEQ ID NO: 6, the complement thereof, SEQ ID NO: 6 with at least one conservative amino acid substitution or its complement; and

introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates the transcription of said DNA in the cell.

31. A method of regulating transcription of the DNA for the receptor of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:

providing a single stranded oligonucleotide at least 10 nucleotides in length, the oligonucleotide being complementary to a portion of the DNA for the receptor of the polypeptide with SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;

providing a cell comprising a DNA for the receptor of the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and

introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates transcription of said DNA in the cell.

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2 32. A method of regulating translation of mRNA for the receptor of the polypeptide of SEQ ID NO:  
3 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:  
4 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
5 oligonucleotide being complementary to a portion of the mRNA that codes for receptor that binds the  
6 polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid  
7 substitution;

8 providing a cell comprising mRNA for the receptor of the polypeptide of SEQ ID NO: 6 or  
9 SEQ ID NO: 6 with at least one conservative amino acid substitution; and

10 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates the  
11 translation of said mRNA in the cell.  
12

13 33. A method of regulating translation of mRNA for the receptor of the polypeptide with the  
14 sequence of SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative  
15 amino acid substitution or the complement thereof comprising the steps of:

16 providing a polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
17 one conservative amino acid substitution;

18 providing a cell comprising mRNA for the receptor of the polypeptide with the sequence of  
19 SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative amino acid  
20 substitution or the complement thereof; and

21 introducing the polypeptide into the cell, wherein the polypeptide regulates the translation of  
22 said mRNA in the cell.  
23

24 34. A method of regulating transcription of the DNA for the receptor of the polypeptide of SEQ ID  
25 NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative amino acid  
26 substitution or the complement thereof, comprising the steps of:

27 providing a polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
28 one conservative amino acid substitution;

29 providing a cell comprising DNA for the receptor of the polypeptide with the sequence of

SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative amino acid substitution or the complement thereof; and

introducing the polypeptide into the cell, wherein the polypeptide regulates the transcription of the DNA in the cell.

35. A method of regulating the function of the receptor to the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:

providing a polypeptide having the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;

providing a cell comprising a receptor to the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and

introducing the polypeptide into the vicinity of the cell, wherein the polypeptide regulates the function of the receptor.

36. A method of regulating transcription of the complement to the DNA for the receptor of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:

providing a single stranded oligonucleotide, 10 nucleotides in length, the oligonucleotide coding for the receptor of the polypeptide with SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;

providing a cell comprising a DNA complementary to the receptor of the polypeptide with SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and

introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates transcription of said DNA in the cell.

37. A method of regulating translation of the complement to the mRNA for the receptor of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:

providing a single stranded oligonucleotide at least 10 nucleotides in length, the



oligonucleotide having a portion of the sequence of the mRNA that codes for the receptor that binds the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;

providing a cell comprising the complement to the mRNA for the receptor of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates the translation of said mRNA in the cell.

38. A method of regulating transcription of the DNA for the receptor that binds the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:

providing a single stranded oligonucleotide at least 10 nucleotides in length, the oligonucleotide being complementary to a portion of SEQ ID NO: 1 or a degenerate variant of SEQ ID NO: 1;

providing a cell comprising DNA for the receptor of the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates transcription of DNA in the cell.

39. A method of regulating translation of mRNA for the receptor of the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:

providing a single stranded oligonucleotide at least 10 nucleotides in length, the oligonucleotide being complementary to a portion of SEQ ID NO: 1 or a degenerate variant of SEQ ID NO: 1;

providing a cell comprising mRNA for the receptor of the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates translation of said mRNA in the cell.

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2 40. A method of regulating secretion of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at  
3 least one conservative amino acid substitution comprising the steps of:

4 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
5 oligonucleotide being complementary to a portion of SEQ ID NO:8 or a degenerate variant of SEQ  
6 ID NO:8;

7 providing a cell comprising mRNA with the sequence of SEQ ID NO: 8 or a degenerate  
8 variant of SEQ ID NO: 8; and

9 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates translation  
10 of said mRNA in the cell.

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12 41. A method of regulating secretion of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at  
13 least one conservative amino acid substitution comprising the steps of:

14 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
15 oligonucleotide being complementary to a portion of SEQ ID NO: 1 or a degenerate variant of SEQ  
16 ID NO: 1;

17 providing a cell comprising a DNA with the sequence of SEQ ID NO: 1 or a degenerate  
18 variant of SEQ ID NO: 1; and

19 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates  
20 transcription of said DNA in the cell.

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22 42. A method of regulating secretion of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at  
23 least one conservative amino acid substitution comprising the steps of:

24 providing a polypeptide having the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
25 one conservative amino acid substitution;

26 providing a cell comprising mRNA with the sequence of SEQ ID NO: 8, the complement  
27 thereof, or a degenerate variant of SEQ ID NO: 8 or its complement; and

28 introducing the polypeptide into the cell, wherein the polypeptide regulates translation of said  
29 mRNA in the cell.

1 43. A method of regulating secretion of the polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at  
2 least one conservative amino acid substitution comprising the steps of:

3 providing a polypeptide having the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
4 one conservative amino acid substitution;

5 providing a cell comprising a DNA with the sequence of SEQ ID NO: 1, the complement  
6 thereof, or the degenerate variant of SEQ ID NO: 1 or its complement ; and

7 introducing the polypeptide into the cell, wherein the polypeptide regulates transcription of  
8 said DNA in the cell.

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10 44. A method of regulating secretion of the receptor to the polypeptide of SEQ ID NO: 6 or SEQ ID  
11 NO: 6 with at least one conservative amino acid substitution comprising the steps of:

12 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
13 oligonucleotide being complementary to a portion of the DNA for the receptor of the polypeptide  
14 with SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;

15 providing a cell comprising a DNA for the receptor of the polypeptide with the sequence of  
16 SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution; and

17 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates  
18 transcription of said DNA in the cell.

19 45. A method of regulating secretion of the receptor to the polypeptide of SEQ ID NO: 6 or SEQ ID  
20 NO: 6 with at least one conservative amino acid substitution comprising the steps of:

21 providing a single stranded oligonucleotide at least 10 nucleotides in length, the  
22 oligonucleotide being complementary to a portion of the mRNA that codes for receptor that binds the  
23 polypeptide of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid  
24 substitution;

25 providing a cell comprising mRNA for the receptor of the polypeptide of SEQ ID NO: 6 or  
26 SEQ ID NO: 6 with at least one conservative amino acid substitution; and

27 introducing the oligonucleotide into the cell, wherein the oligonucleotide regulates the  
28 translation of said mRNA in the cell.

1 46. A method of regulating secretion of the receptor to the polypeptide of SEQ ID NO: 6 or SEQ ID  
2 NO: 6 with at least one conservative amino acid substitution comprising the steps of:

3 providing a polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
4 one conservative amino acid substitution;

5 providing a cell comprising mRNA for the receptor of the polypeptide with the sequence of  
6 SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative amino acid  
7 substitution or the complement thereof; and

8 introducing the polypeptide into the cell, wherein the polypeptide regulates the translation of  
9 said mRNA in the cell.

11 47. A method of regulating secretion of the receptor to the polypeptide of SEQ ID NO: 6 or SEQ ID  
12 NO: 6 with at least one conservative amino acid substitution comprising the steps of:

13 providing a polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
14 one conservative amino acid substitution;

15 providing a cell comprising DNA for the receptor of the polypeptide with the sequence of  
16 SEQ ID NO: 6, the complement thereof, or SEQ ID NO: 6 with at least one conservative amino acid  
17 substitution or the complement thereof; and

18 introducing the polypeptide into the cell, wherein the polypeptide regulates the transcription  
19 of the DNA in the cell.

21 48. A method of regulating the transcription of the mRNA with the sequence of SEQ ID NO: 8 or  
22 SEQ ID NO: 8 with at least one conservative amino acid substitution comprising the steps of:

23 providing a cell comprising a receptor to the polypeptide with the sequence of SEQ ID NO: 6  
24 or SEQ ID NO: 6 with at least one conservative amino acid substitution;

25 binding said polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least  
26 one conservative amino acid substitution to said receptor; and

27 triggering a biological mechanism within said cell responsible for regulating said  
28 transcription.

49. A method of regulating the translation of the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:  
providing a cell comprising a receptor to the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;  
binding said polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution to said receptor; and  
triggering a biological mechanism within said cell responsible for regulating said translation.

50. A method of regulating the secretion of the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution comprising the steps of:  
providing a cell comprising a receptor to the polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution;  
binding said polypeptide with the sequence of SEQ ID NO: 6 or SEQ ID NO: 6 with at least one conservative amino acid substitution to said receptor; and  
triggering a biological mechanism within said cell responsible for regulating said secretion.

51. A purified polypeptide, the amino acid sequence of which comprises SEQ ID NO: 6, SEQ ID NO: 6 with at least one conservative amino acid substitution, or a mimetic functional equivalent of SEQ ID NO: 6.

52. A pharmaceutical preparation comprising a compound according to Claim 51 in admixture with a pharmaceutically acceptable carrier, diluent or excipient.

53. A method of treating a patient or animal, comprising identifying a patient or animal in need of treatment and administering a polypeptide with SEQ ID NO: 6, SEQ ID NO: 6 with at least one conservative amino acid substitution, or a mimetic functional equivalent of SEQ ID NO: 6 to the patient or animal.

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54. A method of treating a patient or animal, comprising identifying a patient or animal in need of treatment and administering a polypeptide which acts as a receptor to the polypeptide of SEQ ID NO: 6, SEQ ID NO: 6 with at least one conservative amino acid substitution, or a mimetic functional equivalent of SEQ ID NO: 6 to the patient or animal.